Reference Material Institute for Clinical Chemistry Standards (ReCCS)

Certified Reference Material for Measurement of Glucose, Creatinine, Uric Acid and Urea-Nitrogen in Human Serum

JCCRM 521-14
Certificate of Analysis

Accredited ASNITE 0006 RMP

■ Intended use

This Certified Reference Material（CRM）is intended primarily for use in calibrating and evaluating the accuracy of routine methods and validating working reference materials. In order to ensure the reliability of evaluation of routine methods, this CRM has three concentration levels: medium, high and abnormally high. Since neither preservatives nor additives are used, and for preparing this CRM fresh serum is used, this CRM shows good commutability to enzymatic methods and chemical quantification methods such as Jaffe method.

Major intended uses are as follows:
(1) To validate working reference materials or calibrators.
(2) To evaluate the accuracy of various routine methods.
(3) To evaluate the internal and external quality of measurements.

■ Instructions for use

(1) Take out a serum vial tube of this CRM and thaw the frozen serum by allowing the tube to stand with the cap-side up at room temperature for approximately one hour.
(2) While holding the serum tube vertically with the cap-side up, hold the cap with fingers, and confirm that the cap is tightly screwed on. If the cap is loose, tighten it securely. Then mix the serum by gently rotating the tube approximately 20 times. Next, turn the tube upside-down slowly at least 40 times to secure homogeneity.
(3) Conduct sampling of the mixed serum for measurements. Unless used immediately, tighten the vial cap and refrigerate it for use in the same day.
Note: Once thawed, the serum should not be frozen again for future use.

■ Precautions for use: In vitro use only

This CRM is prepared from human serum and shown to be negative to the HBs antigens, HCV antibodies and HIV antibodies. However, since other infectious agents are not completely ruled out, handle this CRM as a biohazardous material capable of transmitting infectious diseases.

■ Preparation and Serum property

This CRM was prepared using fresh pooled human serum (ammonium nitrogen is only 0.1 mmol/L as in fresh human serum). It has three concentration levels and the higher levels are prepared by adding high purity creatinine, uric acid, urea nitrogen and glucose into pooled serum. The materials are finally filtrated using 0.2 μm filter for sterilization and securing homogeneity.

■ Storage and expiration

This CRM must be stored in a deep freezer upon receipt.
- 70℃ below : 12 months from shipping date
- 20℃ : 1 months from shipping date

■ Product specifications

A single set of this CRM consists of 6 vials, each vial contains 1.0 mL of human serum. There are 2 vials for each of three different concentration levels indicated below.

- Medium Level JCCRM 521-14M
- High Level JCCRM 521-14H
- Abnormally high Level JCCRM 521-14HH

■ Date of Certification

May 18 , 2023

■ Certified concentration values and uncertainties for Creatinine

The certified concentration values and uncertainties at 25℃ of concentrations of Creatinine are shown below.
Since these analytical measurements were performed at the laboratory in ReCCS as well as observance ISO 17025 and ISO 15195 quality assurance, these values are accepted internationally via ILAC/APLAC MRA.

Accredited
ASNITE 0006 Calibration

Table 1 Certified Concentration Values for Creatinine

	JCCRM 521-14M	JCCRM 521-14H	JCCRM 521-14HH	unit
Creatinine	0.95 ± 0.02	2.24 ± 0.05	5.27 ± 0.10	mg/dL
	84 ± 2	198 ± 4	466 ± 9	μ mol/L

The expanded uncertainty U (95% confidence interval) shown in the above table is obtained by combining standard uncertainty calculated according to the ISO GUM [2]. Uncertainty of SRM and uncertainty of gravimetric method are also included and coverage factor (k) are 2.

■ Certified concentration values and uncertainties for Uric acid, Urea-Nitrogen and Glucose

The certified concentration values and uncertainties at 25℃ of concentrations of Uric acid, Urea-Nitrogen and Glucose are shown below.

Table 2 Certified Concentration Values for Uric acid, Urea-Nitrogen and Glucose

	JCCRM 521-14M	JCCRM 521-14H	JCCRM 521-14HH	unit
Uric acid	5.58 ± 0.12	8.09 ± 0.15	11.82 ± 0.23	mg/dL
	332 ± 7	481 ± 9	703 ± 14	μ mol/L
Urea-Nitrogen *	13.7 ± 0.3	28.5 ± 0.7	45.5 ± 0.9	mg/dL
	4.9 ± 0.2	10.2 ± 0.3	16.2 ± 0.3	mmol/L
Glucose	105.7 ± 2.0	151.5 ± 2.8	244.8 ± 4.4	mg/dL
	5.87 ± 0.11	8.41 ± 0.16	13.59 ± 0.25	mmol/L

*The certified value of urea nitrogen does not include endogenous ammonia nitrogen.

The expanded uncertainty U (95% confidence interval) shown in the above table is obtained by combining standard uncertainty calculated according to the ISO GUM [2]. Uncertainty of SRM and uncertainty of gravimetric method are also included and coverage factor (k) are 2.

■ Traceability to SI units

Traceability for creatinine measurement to SI units was assured via calibration against NIST SRM (Creatinine: SRM 914a, purity 99.7±0.3 %) and consistency was confirmed by comparing with other pertinent standard Materials. Standard solutions and sample solutions used in the measurements were prepared by a gravimetric method using a calibrated balance.

Traceability for Glucose and Urea to SI units was assured via calibration against NIST SRM (Glucose: SRM 917c, purity 99.7±0.2 % and Urea: SRM912b, purity 99.95±0.01 %) and consistency was confirmed by comparing with other pertinent standard Materials.

The HPLC method for uric acid was calibrated with our serum primary reference material for uric acid (JCCRM811) of which values were assayed by the Isotope Dilution Mass Spectrometry in ReCCS.

Standard solutions and sample solutions used in the measurements were prepared by a gravimetric method using a calibrated balance.

■ Measurement methods for certified values

The certified values were determined by the following reference methods by the ReCCS.

- Creatinine: Isotope Dilution Mass Spectrometry according to the NIST measurement procedure for creatinine.〔2〕
- Uric acid: HPLC method after deproteinization.〔3〕
- Urea: The urease-GLD enzymatic method after deproteinization.〔4〕
- Glucose: The hexokinase-G-6-PD enzymatic method after deproteinization. proved to be traceable to ID/MS method (see Fig.1) for glucose.〔5〕

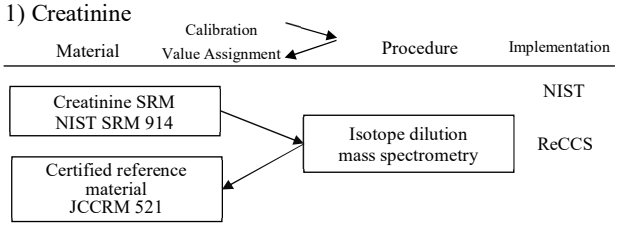
■ Validation of Hexokinase-G-6-PDH reference method by ID/MS

The JSCC reference method for quantification of plasma glucose, hexokinase-G-6-PDH enzymatic method in combination with Somogyi deproteinization method, was evaluated by the deviation from ID/MS. Glucose concentrations of two specimens, 119.2 and 293.6 mg/dL by hexokinase-G-6-PDH were 118.5 and 294.5 mg/dL by ID/MS, respectively; thus the deviations from ID/MS are calculated to be approximately less than relatively 0.5 %, showing that the hexokinase-G-6-PDH method is accurate.

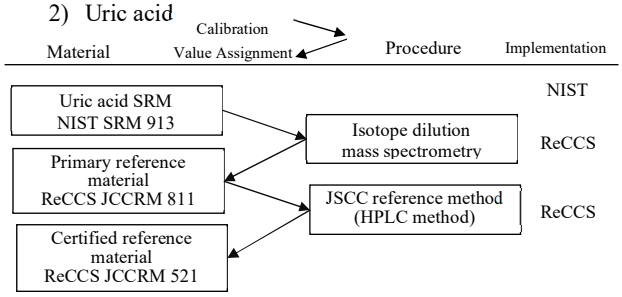
■ Traceability to the SI unit

Calibration transfer protocols for giving metrological traceability to the SI unit are as follows.

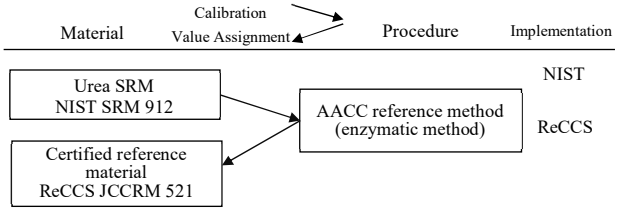
1) Creatinine



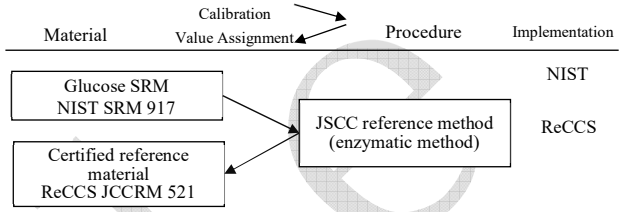
2) Uric acid



3) Urea-Nitrogen



4) Glucose



■ Characteristics of This CRM

The characteristics of this CRM are as follows.

Item	JCCRM 521-14	unit	Method
Ammonia nitrogen	0.1	mmol/L	Colorimetric method
Total protein	7.2	g/dL	Biuret method
Albumin	4.4	g/dL	BCG colorimetric method
Total cholesterol	172	mg/dL	Enzymatic method
Triglycerides	106	mg/dL	Enzymatic method
Density	1.024 (25 ℃)	g/cm^3	

■ References

〔1〕 Evaluation of measurement data - Guide to the expression of uncertainty in measurement, ISO/IEC Guide 98-3 (JCGM 100:2008).
〔2〕 Dodder NG, Tai SS, Sniegoski LT, Zhang NF, Welch MJ : Certification of creatinine in a human serum reference material by GC-MS and LC-MS, Clin Chem, 53(9) : 1694-1699, 2007.
〔3〕 Reagent Committee, Japan Society of Clinical Chemistry: Recommended Methods for the measurement of Serum Uric Acid using HPLC Rinsho Kagaku, 22 : 300-307, 1993.
〔4〕 Sampson EJ, Baird MA, Burtis CA, Smith EM, Witte DL, Bayse DD, A Coupled-Enzyme Equilibrium Method for Measuring Urea in Serum: Optimization and Evaluation of the AACC Study Group on the Urea Candidate Reference Method, Clin Chem 26 : 816-826, 1980.
〔5〕 Reagent Committee, Japan Society of Clinical Chemistry: Recommended methods for measuring serum glucose, Rinsho Kagaku,, 20 : 247-254, 1991.

Provider of JCCRM 521-14

Hirohito Umemoto Ph.D.

Hirohito Umemoto, Ph.D. (President)

Certificate Revision		
R0	2019.7.11	Original certificate issue date
R1	2020.9.4	ISO Guide 34 to ISO 17034
R2	2021.7.15	Contact modification
R3	2023.5.18	Uncertainty change

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